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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,561	03/21/2005	Yoshiharu Minamitake	58778.000003	7719

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EXAMINER

GUDIBANDE, SATYANARAYAN R

ART UNIT	PAPER NUMBER
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1654

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/500,561

Applicant(s)

MINAMITAKE ET AL.

Examiner

Satyanarayana R. Gudibande

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 July 1219.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 1-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892).
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

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DETAILED ACTION

Applicant's amendments to claims in the response filed on 12/19/06 have been acknowledged.

Claims 1-27 are pending.

Claims 1-16 have been withdrawn from further consideration as being drawn to non-elected invention.

Claims 17-27 are examined on the merit.

Any objections and rejections not specifically mentioned here is considered withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17-27 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Matsumoto, et al., Biochemical and biophysical Research communications, 2001,287, 142-146 in view of US 6,967,237 B2 issued to Bednarek, and further in view of Voet, et al., Biochemistry, 1995, II Edition, John Wiley & Sons, Inc., pages 60-62 and 77 as stated in our previous office action dated 9/22/06.

Applicants argue that cited references alone or in combination fail to teach or suggest every claim limitation and the references do not teach or suggest adjusting the pH of the solution comprising ghrelin or its derivative in the range of from 2-7. Applicants further argue that the references fail to teach limitations in each dependent claim, for example, the concentration of the pH adjuster or the buffer agent is in the range 0.01 mM to 1000 mM.

Applicants argue that neither the '237 patent nor Voet teach or suggest a positive charge in a ghrelin molecule is maintained by converting the ghrelin molecule to an acid salt'. Furthermore, the Office Action has not shown where in the references the "motivation for maintaining the pH in the range of 2-7" is found. In addition, neither the '237 patent nor Voet provide any suggestion or motivation to modify Matsumoto by adjusting the pH of a solution for any reason, and in particular, to prevent degradation of a hydrophobic group of ghrelin or its derivative.

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Applicants further argue that the office does not provide any evidence to support the statement that "given the knowledge that protonated ghrelin molecules would have higher activity combined with the hydrophobicity at the 3rd residue at the N-terminal end."

Applicant's arguments filed 12/19/06 have been fully considered but they are not persuasive. In the instant application, applicants claim a method of preventing degradation of a hydrophobic group of ghrelin or its derivative in a solution with a pH in the range 2 to 7. Applicants also claim acetic acid as pH adjuster and acetate buffer as buffer solution.

With regards to applicant's argument that references alone or in combination do not suggest adjusting the pH of the solution comprising ghrelin or its derivative in the range of from 2-7 is not persuasive because the reference of Matsumoto clearly states that positive charges are essential in maintaining high level activity of the ghrelin and negative charges inhibit activity (Matsumoto, column 2, paragraph 1, page 145). It is implicit that positive charge on a protein or a peptide is achievable only by protonation as shown by Voet reference and protonation of protein or peptide is possible when the pH is maintained below pH 7.

With regards to argument about the range of pH being in the range 2-7 and concentration of the pH adjuster being in the range of 0.01 to 1000 mM, the MPEP states that "[G]enerally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is **critical**. The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages" see MPEP 2144.05.

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With regards to argument that references does not teach or suggest a positive charge in a ghrelin molecule can be maintained by converting the ghrelin molecule to an acid salt and no motivation for maintaining the pH in the range 2-7 is not persuasive either. Because, addition of an acid such as acetic acid and buffering agent such as acetate, the protein is protonated and remains protonated as shown by Voet reference and the motivation to do so is clear from the Matsumoto reference because the reference of Matsumoto clearly states that positive charges are essential in maintaining high level activity of the ghrelin and negative charges inhibit activity.

With respect applicant's argument that the office does not provide any evidence to support the statement that "given the knowledge that protonated ghrelin molecules would have higher activity combined with the hydrophobicity at the 3rd residue at the N-terminal end", Masumoto reference clearly state that "the potency of both [Nle³]-human ghrelin and [Lys³] was increased to an EC₅₀ of 120 nM simply by adding n-butyl for Nle and n-butylamine for Lys and the elimination of positive charges at the N-terminus of ghrelin lowered the ghrelin activity (page 145, column 2, paragraph 1).

Therefore, the rejection of claims 17-27 is proper under 35 USC 103 and is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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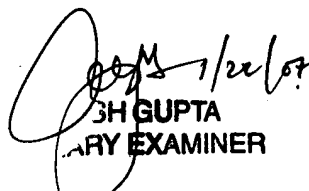
the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Satyanarayana R. Gudibande, Ph.D.
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SH GUPTA
ARY EXAMINER